Neuroscience Module

Lecture (6)

Role of amino acids derivatives in CNS metabolism

By

Enas Samir Nabih

Professor of Medical Biochemistry and Molecular Biology

Lecture Key points

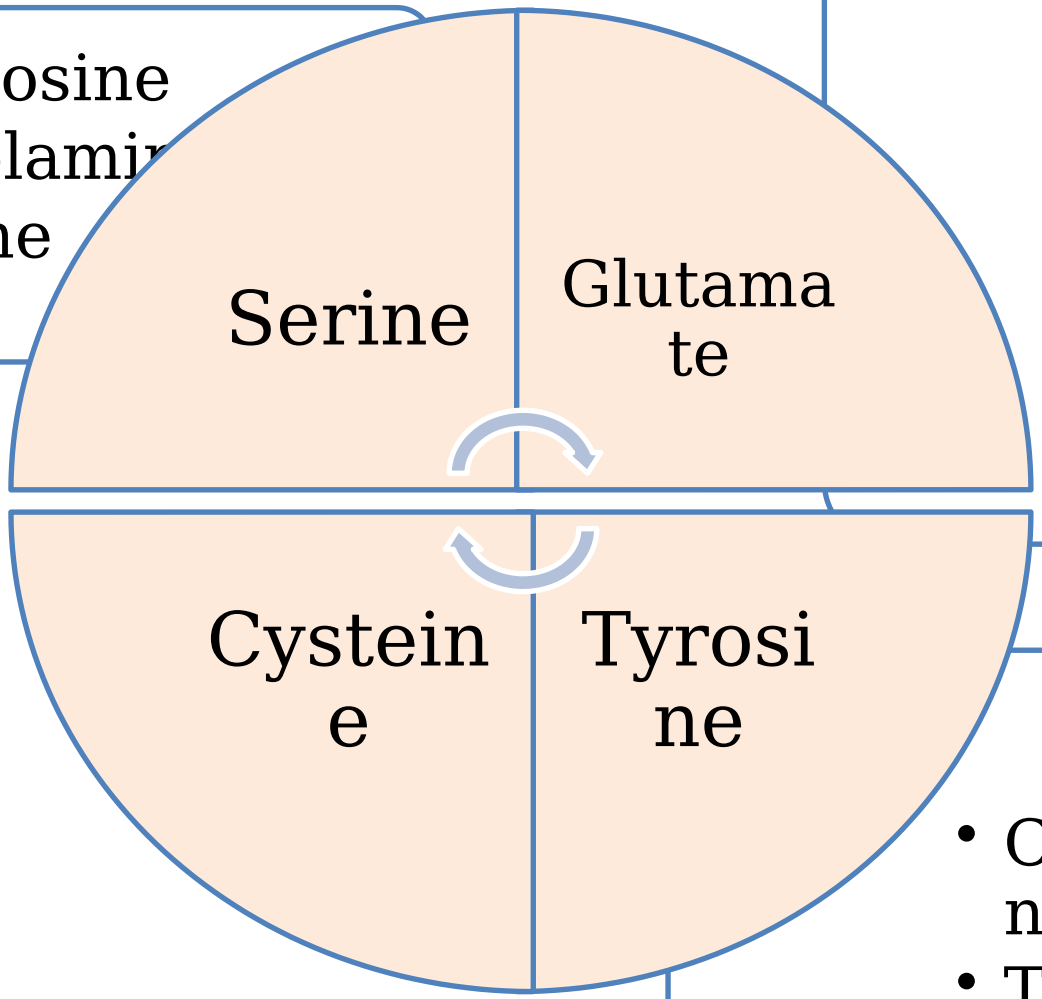
- The metabolism and clinical significance of important compounds derived from amino acids

INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Categorize compounds derived from amino acids
2. Explain with illustration the synthesis and degradation of important compounds derived from amino acids
3. Discuss clinical importance of compounds derived from amino acid metabolism

Outlines



- Sphingosine
- Ethanolamin
- Cysteine

- GABA
- Glutamin e
- N-acetyl glutamic acid
- Proline and arginine
- GLa
- GSH

- Catecholami nes
- Thyroid hormones

Amino acids

Amino Acid Requirements of Humans	
Nutritionally Essential	**Nutritionally Nonessential**
Arginine[a]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Proline
Tryptophan	Serine
Valine	Tyrosine

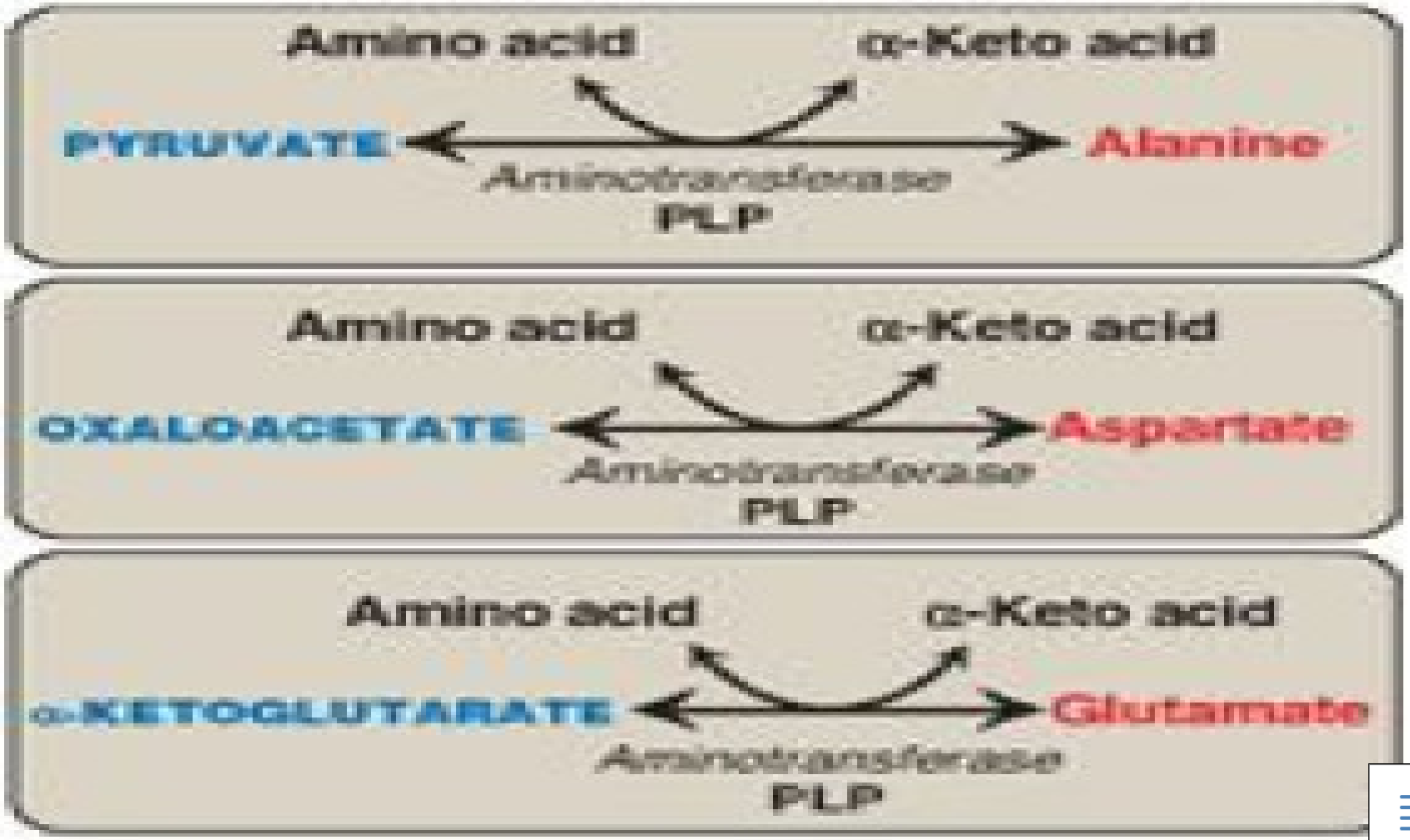
[a] "Nutritionally semiessential." Synthesized at rates inadequate to support growth of children.

Synthesis of non-essential amino acids

1) • **From α-keto acids: By transamination**
2) • **Synthesis of glutamine and asparagine: By amidation**
3) • **Proline and arginine: From glutamate**
4) • **Serine: From 3-phosphoglycerate and glycine**
5) • **Cysteine**
6) • **Tyrosine: From phenyl alanine**

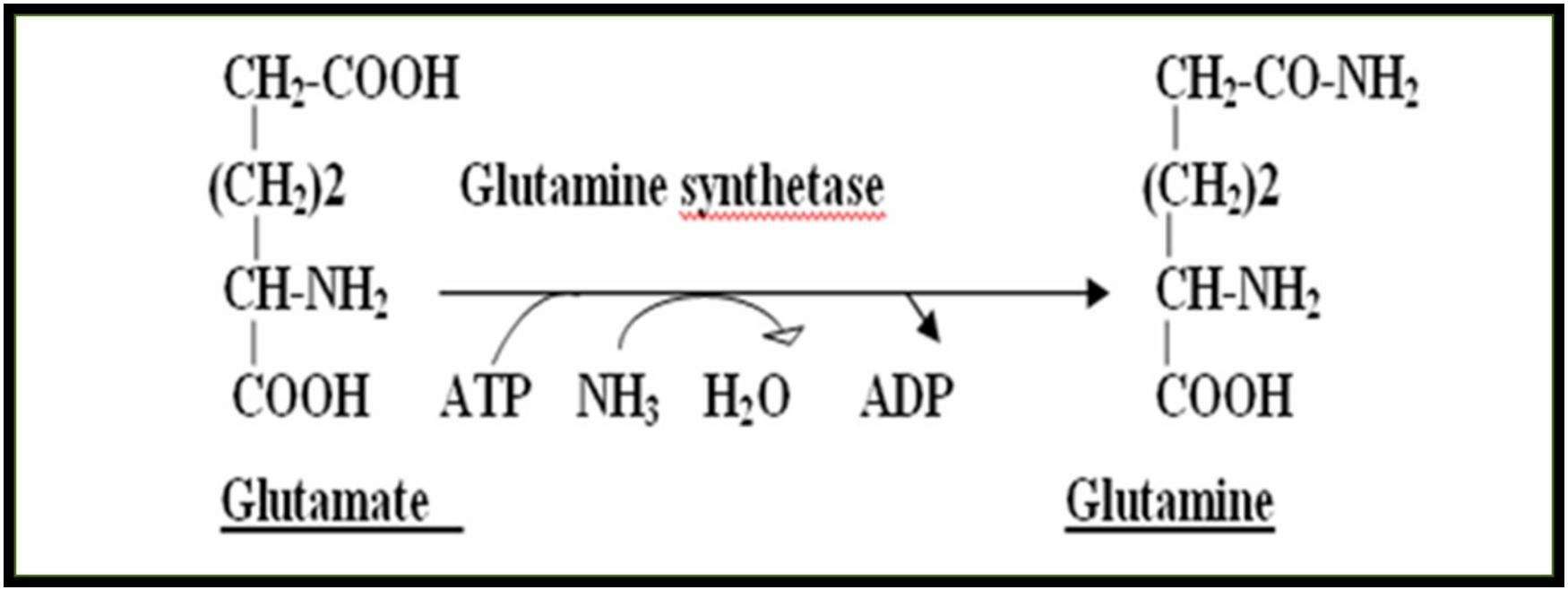
Synthesis of non-essential amino acids

1) By transamination (From α-keto acids):
Glutamate, aspartate and alanine



Lippincott's illustrated reviews in Biochemis

Synthesis of non-essential amino acids
2) By amidation: glutamine and asparagine

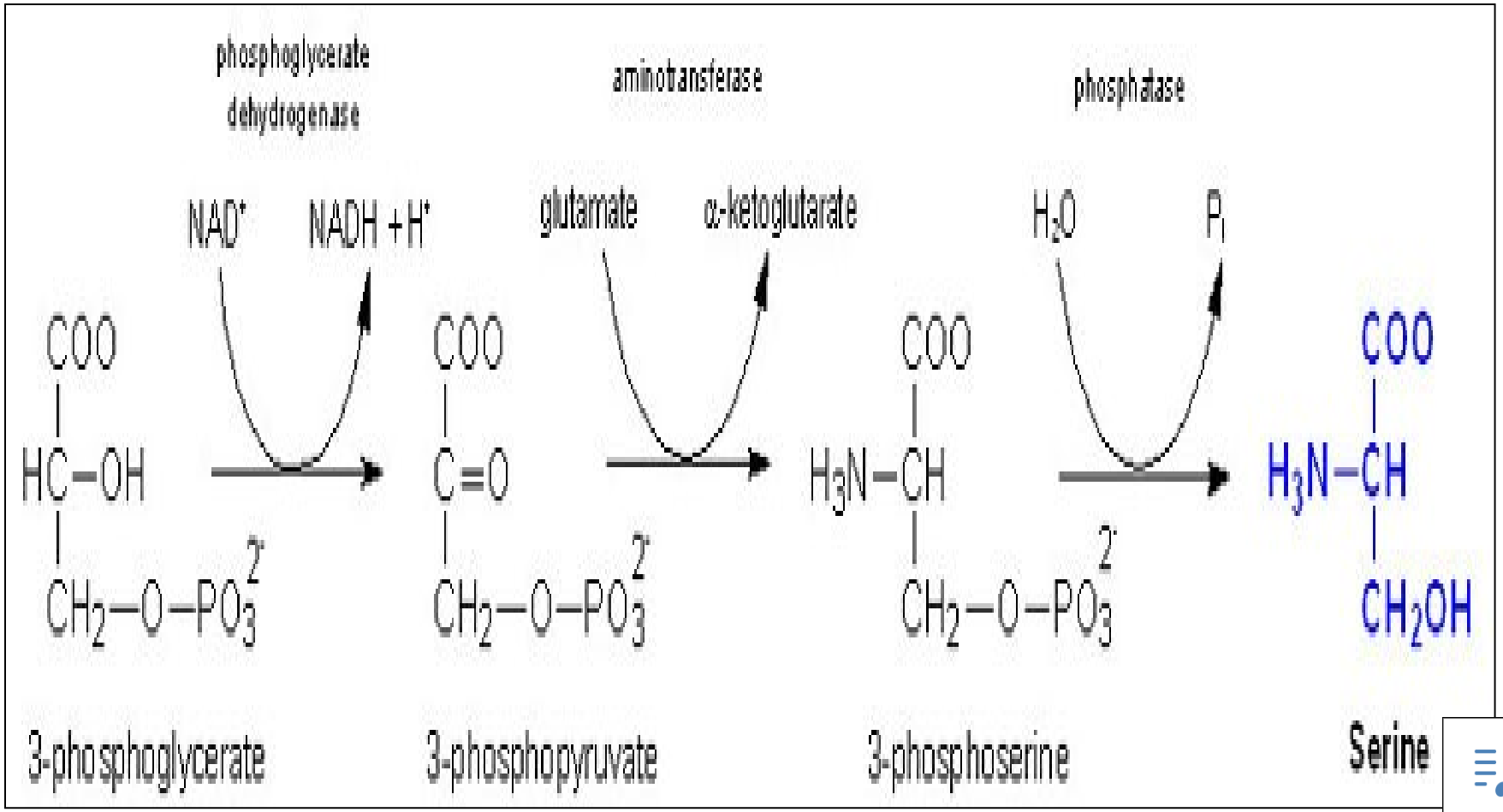


https://www.google.com/search?hl=en-US&biw=1366&bih=662&tbm=isch&sa=1&ei=GMFXXemwHYeWlwSkrID4CA&q=Glutamine+synthetase&oq=Glutamine+synthetase&gs_l=img.3..0l10.38790.45678..46780...0.0..0.350.5860.0j23j6j2.....0....1..gws-wiz-img.....0i67j0i5i30.YDIRnmZVfsE&ved=0ahUKEwjpnJ-xxInkAhUHy4UKHSQWAI8Q4dUDCAY&uact=5

Synthesis of non-essential amino acids

3) Biosynthesis of Serine

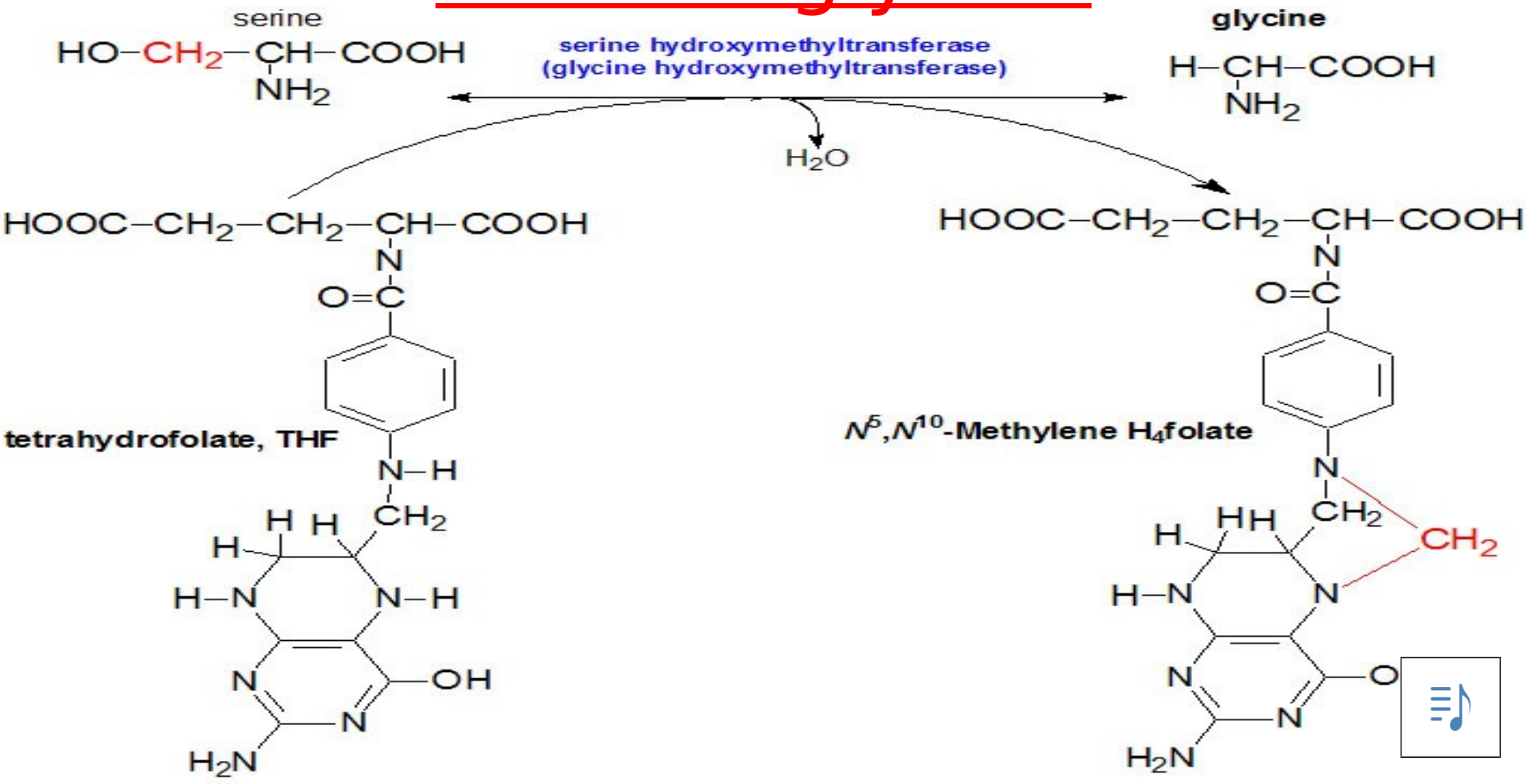
A) From 3-Phosphoglycerate (major source of serine)



Synthesis of non-essential amino acids

3) Biosynthesis of Serine

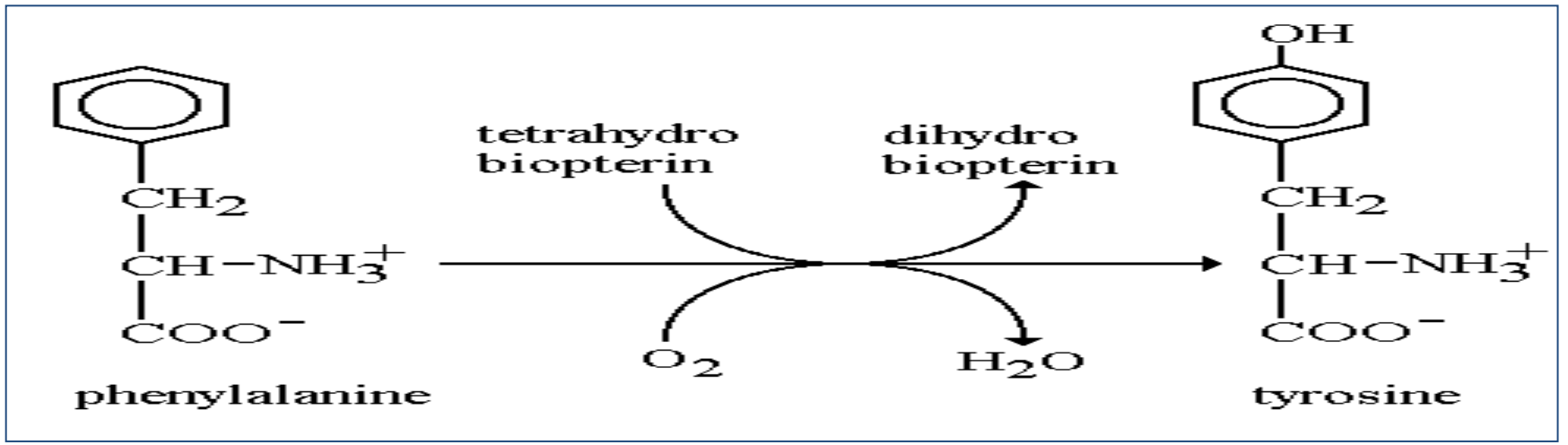
B- From glycine



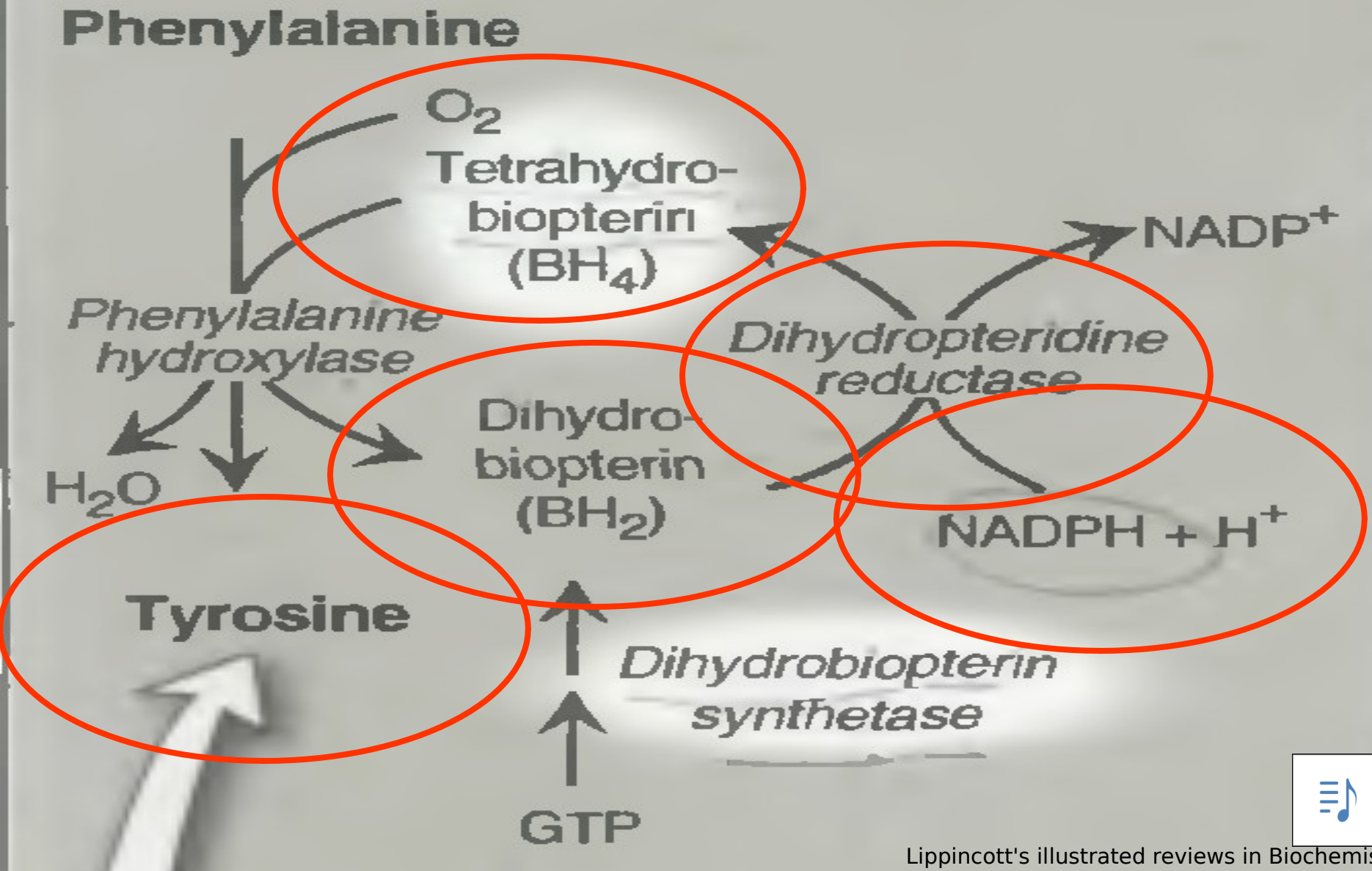
Synthesis of non-essential amino acids

4) Biosynthesis of tyrosine from phenyl alanine

Catalyzed by the enzyme phenylalanine hydroxylase.

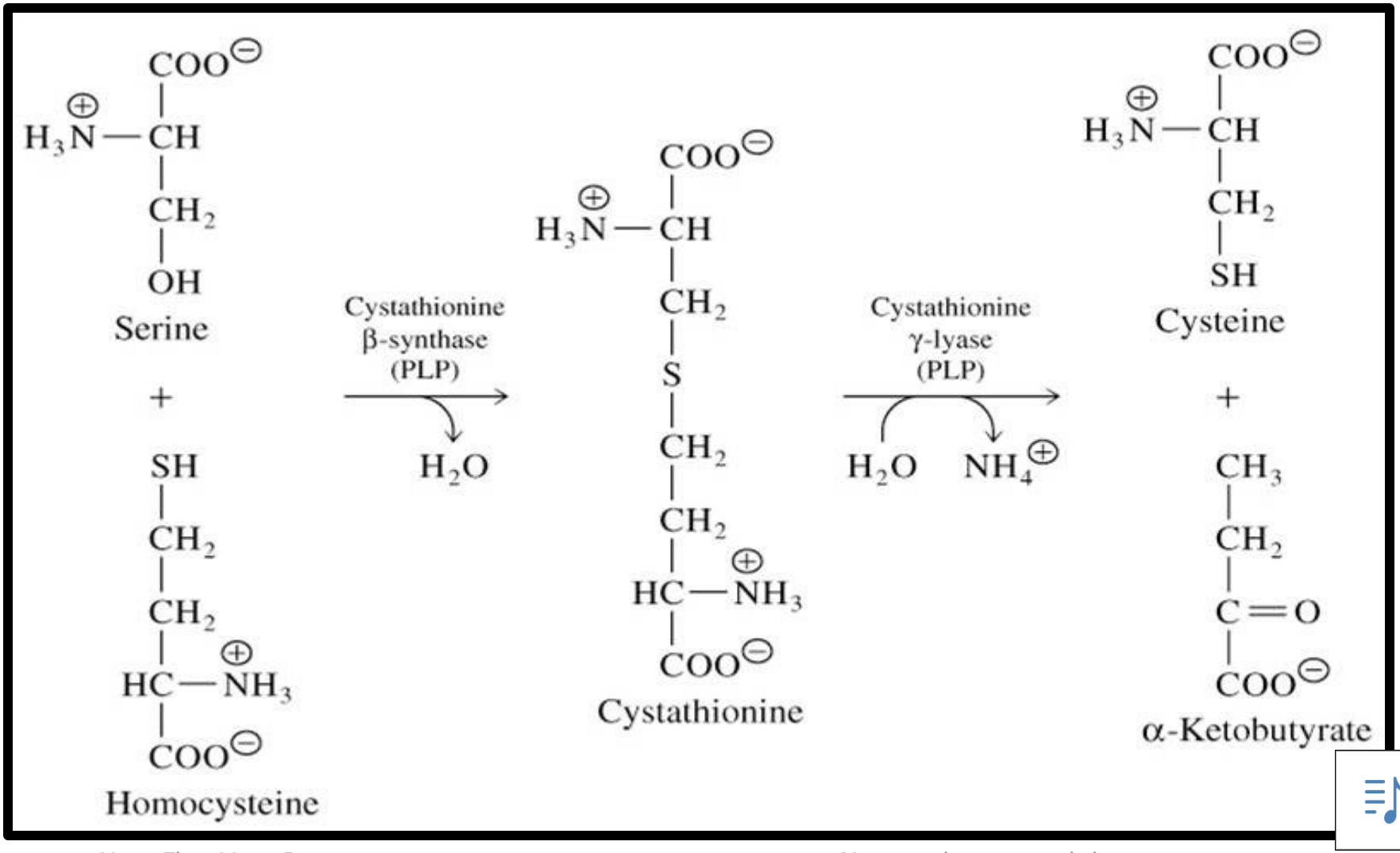


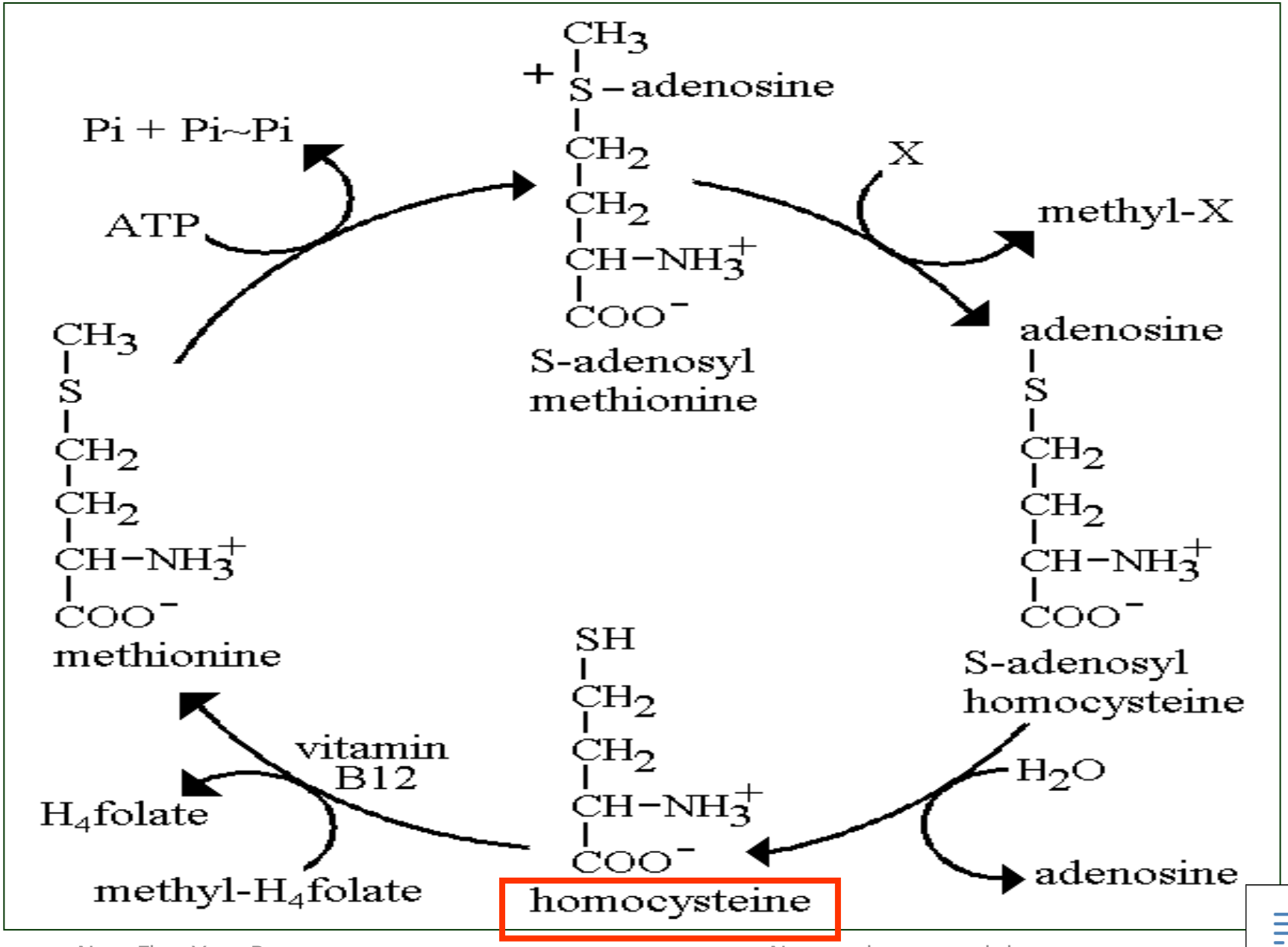
Tyrosine synthesis



Synthesis of non-essential amino acids

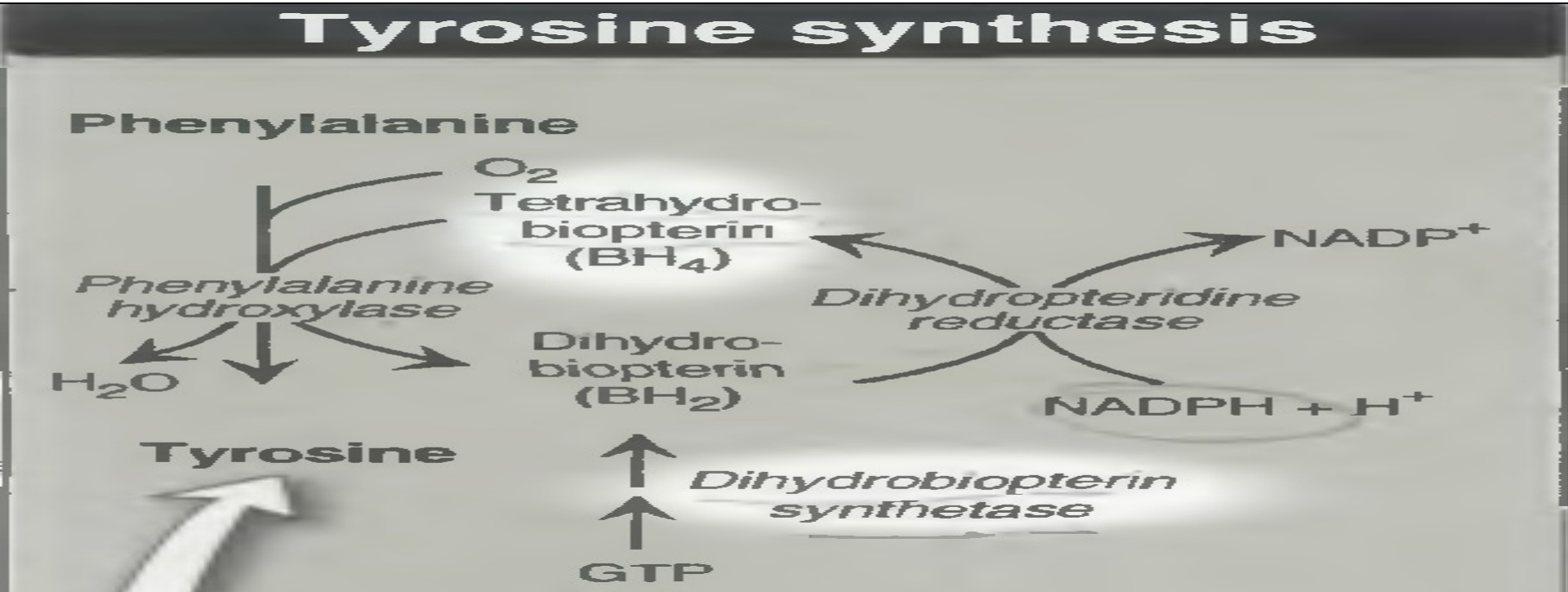
5) Biosynthesis of cysteine from serine




Pi + Pi~Pi
ATP
S-adenosyl
methionine
X
methyl-X
adenosine
S-adenosyl
homocysteine
H2O
adenosine
homocysteine
vitamin
B12
H4folate
methyl-H4folate
methionine

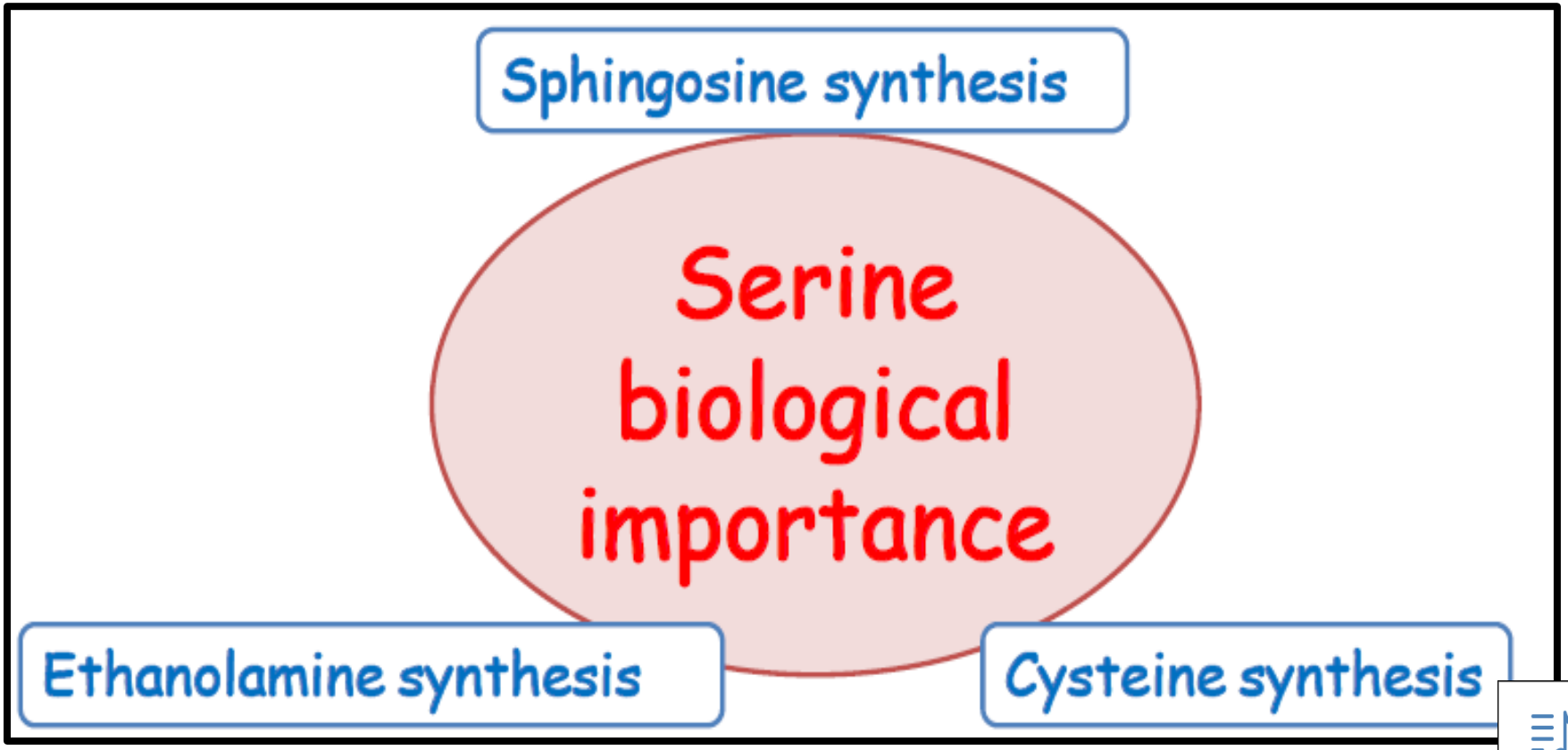
The metabolism and clinical significance of important compounds derived from amino acids (Quiz)

- Illustrate the synthesis of tyrosine from phenylalanine

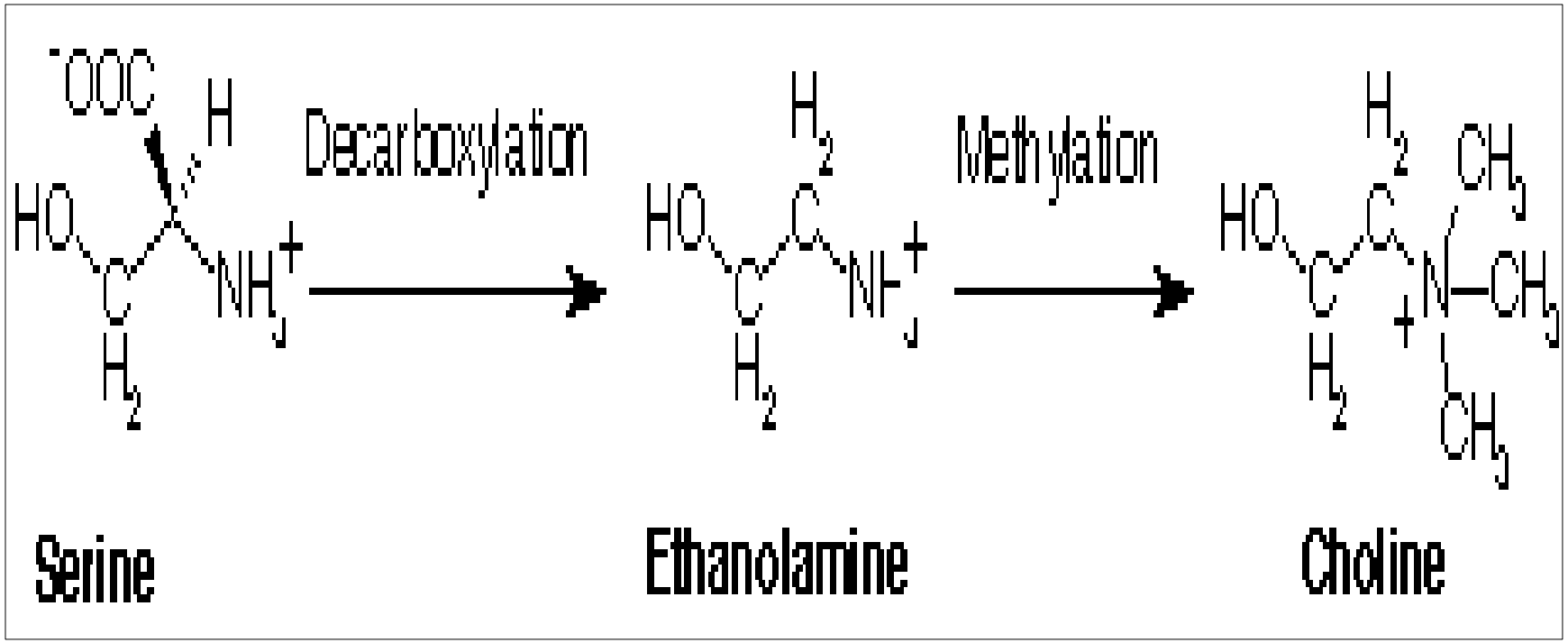


Biological compounds derived from amino acids

1) Serine:



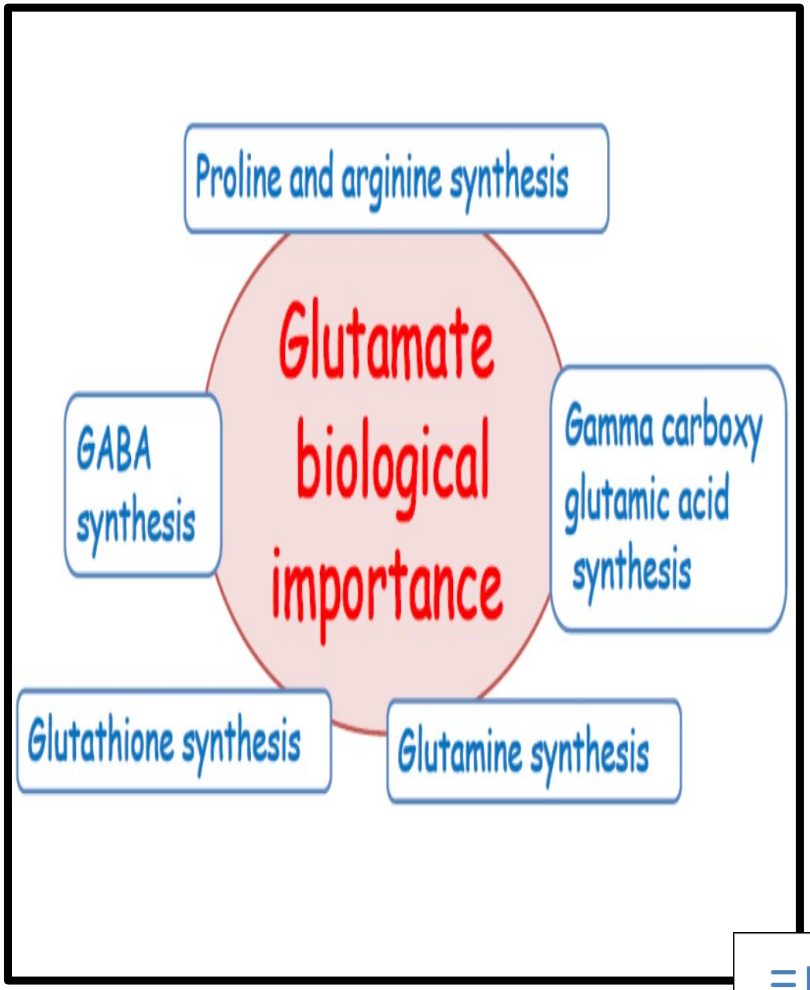
Ethanolamine



Biological compounds derived from amino acids

2) Glutamate:

- GABA (Refer to neurotransmitters)
- Glutamine
- N-acetyl glutamic acid
- Proline and arginine
- Gamma carboxyglutamic acid
- Glutathione



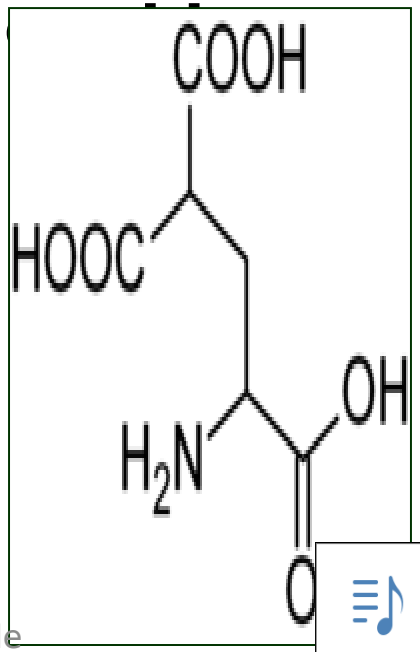
Gamma carboxyglutamic acid

- **It is a glutamic with 2 COOH at its radical.**
- **Formed by carboxylation of glutamic at the γ-carbon on several calcium-dependent proteins (clotting factors II, VII, IX, and X and the anticoagulant proteins protein C and protein S) forming γ-carboxyglutami**

- This process is vitamin K dependent.

- **γ-carboxyglutamic acid**

chelates calcium ions which permits the binding of the blood-clotting proteins to membranes.



Biological compounds derived from amino acids

3) Tryptophan:

- Serotonin and melatonin

(Refer to neurotransmitters)

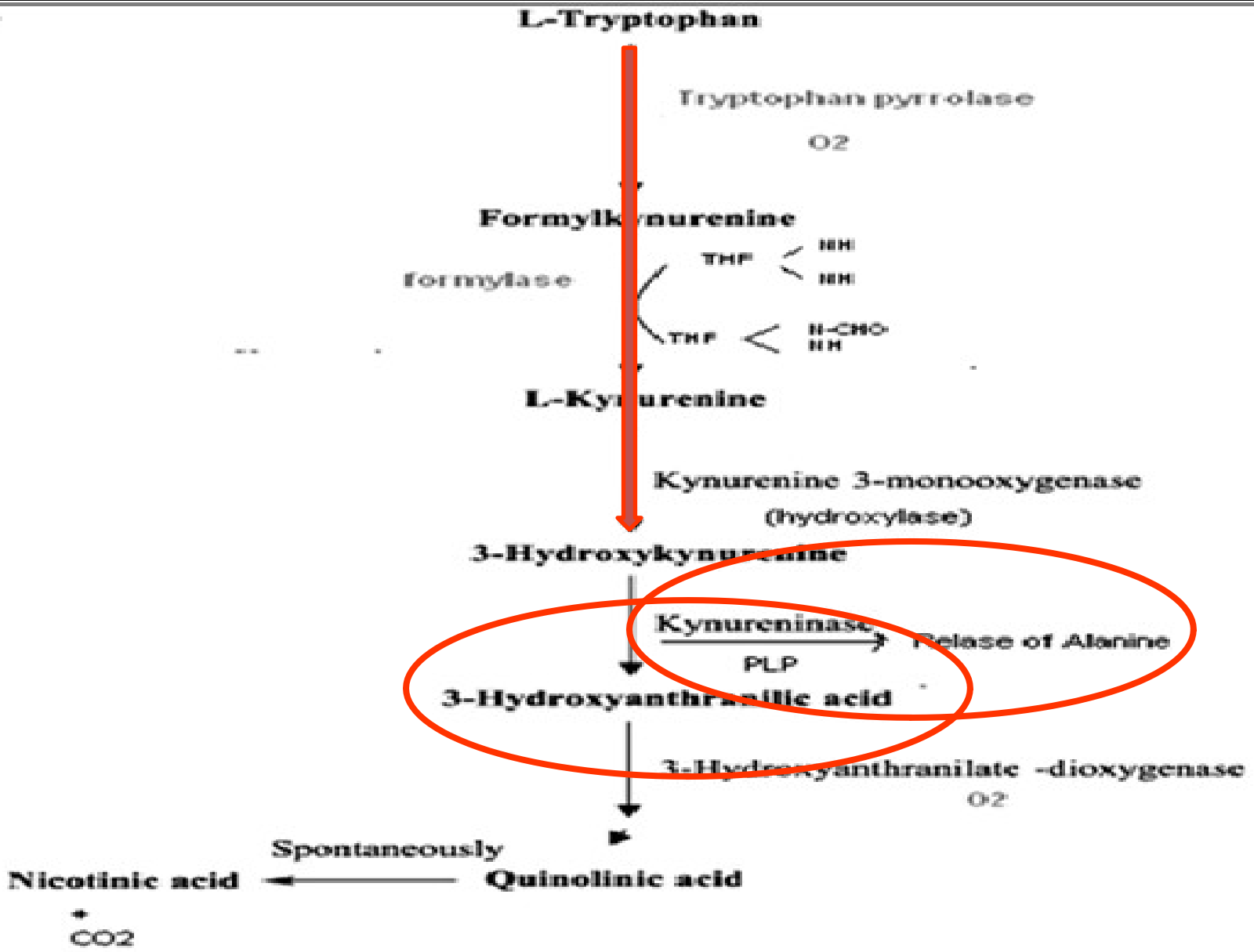
- Nicotinic acid

Nicotinic acid

- The major metabolic fate of tryptophan in the body is to be oxidized by tryptophan pyrrolase

- Tryptophan pyrrolase is a hemeprotein, induced by corticosteroids and increase tryptophan in diet.

Biosynthesis of nicotinic acid (NIACIN)

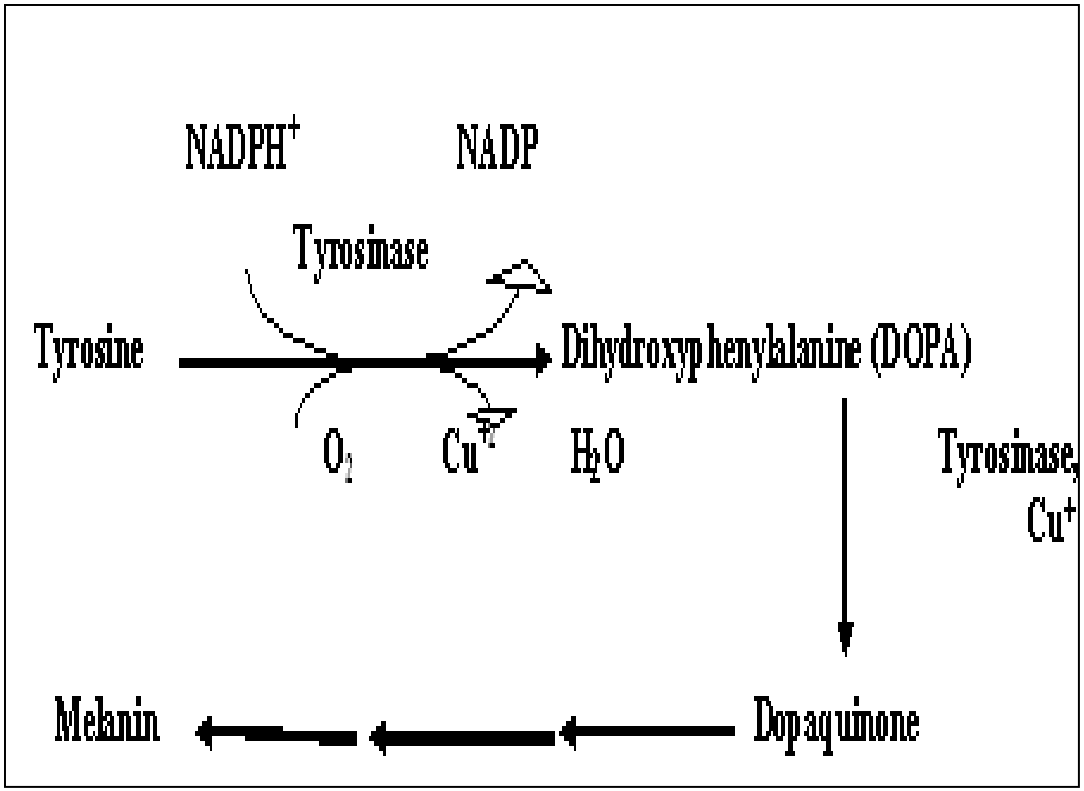


Biological compounds derived from amino acids

4) Phenylalanine and tyrosine:

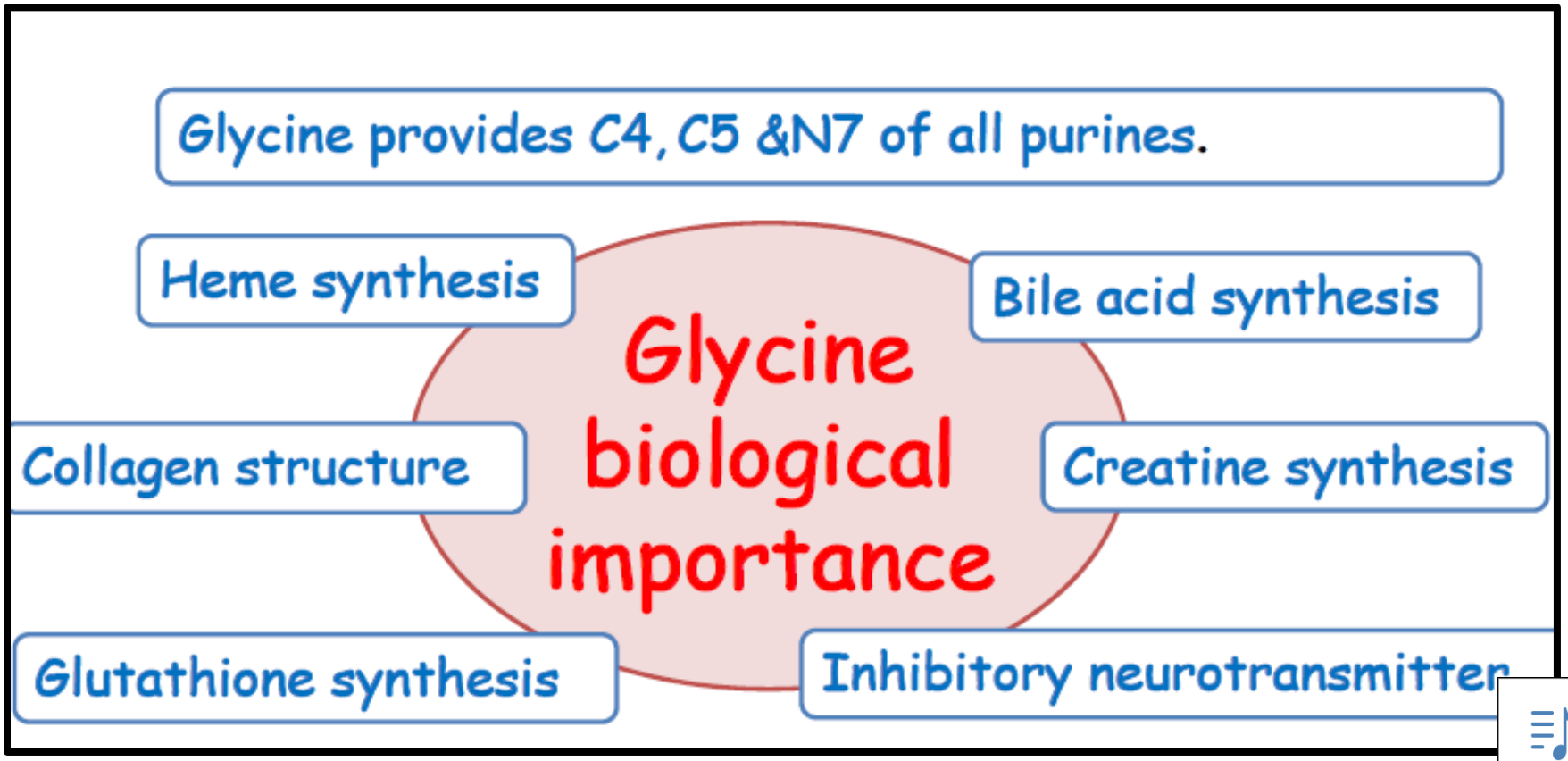
- Catecholamines (Refer to neurotransmitters)
- Thyroid hormones (Refer to T3 and T4 synthesis)
- Melanin

Synthesis of Melanin pigment in (melanocytes)



Biological compounds derived from amino acids

5) Glycine:



Lecture Quiz

USMLE Question

A 62-year-old woman presents to the clinic complaining of frequent bleeding while brushing her teeth and easy bruising. She reports she recently had pneumonia and was treated with a broad-spectrum antibiotic. Laboratory tests show:

Prothrombin time: 18 seconds
Partial thromboplastin time: 37 seconds
Platelet count: 231,000/mm^3
Hematocrit: 37%
WBC count: 4800/mm^3

The cofactor that is deficient in this patient is needed for the carboxylation of glutamate residues of which of the following?

(A) Factors II, VII, VIII, and X
(B) Factors VII, VIII, IX, and XII
(C) Proteins C and S and factors IX, X, XI, and XII
(D) Proteins C and S and factors XII, IX, and
(E) Proteins C and S, prothrombin, and factors VII, IX, and X

Summary

-Nutritionally essential and non-essential amino acids
-Synthesis of non-essential amino acids
-The clinical significance of important compounds derived from amino acids

SUGGESTED TEXTBOOKS

- **Lippincott's illustrated reviews in Biochemistry by P.C. Champe, R.A. Harvey and D.R. Ferrier**
- **Fundamentals of Clinical Chemistry (Tietz)**
- **"Textbook of Biochemistry with Clinical Correlations" by T.M. Devlin**
- **"Harper's Biochemistry" by R.K. Murray, D.K. Granner, P.A. Mayes and V.W. Rodwell**

THANK YOU